REMARKS

Applicant gratefully acknowledges the courtesy of a personal interview on May 10, 2004, in which Examiner Fay and Minh-Quan K. Pham discussed the pending prior art rejection. During the interview, the Hills (WO 91/12808) reference was discussed with regard to the claims. The Examiner agreed to consider evidence showing that the reference taught away from the present invention.

The Office Action mailed September 23, 2004, has been carefully considered. The present Response is intended to be a complete reply thereto and to place the case in condition for allowance.

Claims 108-109, 112-113, 115-130, and 132 are pending. Claims 1-107, 110-111, 114, 131, and 133-140 have been cancelled.

THE CLAIMS ARE NOT OBVIOUS

Claims 108, 109, and 116 stand rejected under 35 U.S.C. § 103(a) as being obvious over Hills (WO 91/12808). Applicant respectfully traverses the rejection.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *See* MPEP 2143.

First, Hills fails to teach or suggest all the claim limitations. In particular, Hills fails to disclose the diseases recited by claim 108. The reference describes the use of phospholipids,

optionally with hyaluronic acid (HA), as a tear substitute material for lubrication of the eye. On page 3, 6th full paragraph, Hills specifically discloses that the "solution is used as a lubricant between the eyelid and the ocular surface or contact lens." The present invention relates to a totally different group of eye diseases that are not necessarily involved in the manifestation of dry eye needing lubrication, i.e. the disease concerned with by the present invention may occur even under conditions where there is a natural process of lubrication of the eye. The present invention provides for a healing effect on corneal epithelial cells. The healing effect regenerates cells whenever the cells are lacking or damaged, notwithstanding whether the natural lubrication process within the eye has been damage. There is no teaching in Hills that phospholipids or any other component of the present invention may be used for any other purpose other than the lubrication of dry eye.

Moreover, Hills actually teaches away from using phospholipids to effect healing of the corneal epithelium upon tissue damage. In other words, Hills teaches away from the present invention. This is evidenced throughout the disclosure of Hills. First, the reference discloses a preferred composition having HA (see page 3, 5th full paragraph). Applicant respectfully submits herewith an abstract of a publication by Harizman et al. (*Investigative Ophthalmology & Visual Science* 44:U328-U328 3826 Suppl. 2, May 2004) which shows that, although HA improves eye lubrication and breaking time, it actually delays healing of corneal erosion. This is clearly inapposite to the present invention which promotes corneal healing. Although Hills recited HA as an optional component, the use of phopholipids in combination with HA would have led one of ordinary skill in the art to the conclusion that Hills does not contemplate the use of phospholipids for corneal healing.

Second, the examples provided in the cited reference could not have suggested any healing effect of the agent used according to the present invention. Specifically, the experiments use eyes from freshly killed sheep (Example I) and ball bearings (Example II). It is obvious, therefore, that Hills does not contemplate any healing effect, because cell proliferation (part of the healing process) cannot occur in a model obtained from dead animals or from ball bearings. It is clear from the examples that the Hills' composition is intended merely as an eye lubricant. No healing effect is contemplated or suggested. As discuss above, Hills actually teaches away from any healing effect by preferably using HA.

Therefore, because Hills fails to disclose every element of and teaches away from Applicant's claimed invention, the reference does not render the claims obvious under the meaning of 35 U.S.C. § 103. Accordingly, Applicant respectfully requests withdrawal of the rejection.

ALLOWABLE SUBJECT MATTER

Because claims 112, 113, 115, 117-130 and 132 are not rejected over the prior art, these claims remain allowable if rewritten in independent form.

CONCLUSION

Applicant has responded to the Office Action mailed September 23, 2004. All of the claims are now believed to be allowable and favorable action is respectfully requested.

In the event that there are any questions relating to this Response or to the application in general, it would be appreciated if the examiner would telephone the undersigned attorney concerning such questions so that the prosecution of this application may be expedited.

Please charge any shortage or credit any overpayment of fees to BLANK ROME LLP, Deposit Account No. 23-2185 (000744-00077). In the event that a petition for an extension of time is required to be submitted herewith and in the event that a separate petition does not accompany this response, applicant hereby petitions under 37 C.F.R. 1.136(a) for an extension of time for as many months as are required to render this submission timely.

Any fees due are authorized above.

Respectfully submitted,

Date: Dec 21, 2004 By: _____

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Full Record

Record 4 of 12 | SUMMARY

Title: The effect of healon5 on the healing speed of corneal erosions in an animal model

Author(s): Harizman N, **Belkin M**, Rosner M

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Association for Research in Vision and Ophthalmology, May 4 - 9, 2003, Ft. Lauderdale, Florida

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The Effect of Healon5 on the Healing Speed of Corneal Erosions in an Animal Model

N.Harizman, M.Belkin, M.Rosner. Goldschleger Eye Research Institute, Tel-Aviv University, Sheba Medical Center, Tel-Hashomer, Israel.

Purpose: Hyaluronic acid was proved to enhance corneal re-epithelization in vitro and in vivo. Healon5, a new drug based on hyaluronic acid, is used to protect endothelial cells during intraocular surgery. An animal model study was conducted to evaluate the effect of healon5 on the healing speed of corneal erosions.
Methods: Corneal erosions, six millimeter in diameter, were induced in one eye of 15 rabbits. Five rabbits were treated with healon5, five rabbits with Chloramphenicol 5% ointment and five other rabbits served as the untreated control group. The corneas were evaluated, photographed and treated at 8 hour intervals until full healing of the erosion was observed. The erosion area was calculated from photographs using a computerized photograph analyzer. After the erosion was completely healed, the rabbits were sacrificed and histopathologic examination of the corneas was performed.
Results: The mean healing time of the corneal erosions was 82 hours for the group treated by Healon5, 68.8 hours for the Chloramphenicol 5% ointment treatment group, and it was the shortest, 54.4 hours, in the untreated control group. The differences between the Healon5 or the ointment treatment groups and the untreated control group were statistically significant (t test: P=0.00003, P=0.05, respectively). The histopathologic evaluation of the healed corneas revealed no significant difference between the three groups.
Conclusions:
Healon5 caused a significant delay in the healing of corneal erosions, and thus it is not suitable for artificial bandaging of corneal erosions. It was shown that ointments such as Chloramphenicol 5% also delayed the healing of corneal erosions compared to the rate of healing with no treatment at all.
Commercial Relationship: N. Harizman, None; **M. Belkin**, None; **M. Rosner**, None.

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Keyword, Presentation and Grant ID (Complete):
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(1) : 372 cornea: epithelium
(3) : 316 animal model
(2) : 632 wound healing
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